REMARKS

Box 4 of the Office Action Summary indicates that claims 1-4, 8-10, 13-21, 23 and 25 are pending; however, Applicant notes that claims 1-25 are in fact currently pending in this application. Claims 5-7, 11-12, 22 and 24 have been withdrawn from consideration and canceled. Claims 1-4, 8-10, 13-21, 23 and 25 have been rejected. Claims 1-2, 4, 8-9, 13, 16, 19, 23 and 25 have been amended in response to claim rejections and to correct informalities. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. Election/Restriction Requirement Under 35 U.S.C. §121

The election of Group I, claims 1-4, 8-10, 23 and 25 has been acknowledged. Further, in light of Applicant's arguments in the reply filed July 28, 2004, the Examiner has also examined Group III (claims 13-21), wherein the claims of Group III are limited to a method comprising identifying agents which inhibit the expression of the nucleic acid of Group I. Claims 5-7, 11, 12, 22 and 24 have been withdrawn from further consideration. Accordingly, Applicant is canceling these claims without prejudice, reserving the right to file continuing applications for this subject matter.

II. Rejection of Claims under 35 U.S.C. §101, Double Patenting

Claims 1-4, 8-10, 13-21, 23 and 25 have been provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-4, 8-10, 13-21, 23 and 25 of copending Application No. 10/469,477. An election of claims for copending

Application No. 10/469,477 has not been made and Applicant will make an effort to avoid electing claims for the '477 application which overlap with the claims of the instant application.

Claim 19 has also been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 8 and 9 of copending Application No. 10/290,142. As copending Application No. 10/290,142 has been abandoned, it is respectfully requested that this rejection be withdrawn.

Claims 1-4 have been rejected under 35 U.S.C. 101 because they are non-statutory. Adding "isolated" or some similar recitation has been suggested to overcome this rejection. Accordingly, Applicant has amended claims 1 and 4, and by dependency claims 2 and 3, to recite that the claimed nucleic acids are isolated. It is therefore respectfully requested that this rejection be withdrawn.

III. Objections to the Specification

The specification has been objected to for the recitation of "Awhich...processes@" at page 3, lines 11-12. Applicant has amended the specification to correct the inadvertent typographical errors. Withdrawal of this objection is therefore respectfully requested.

IV. Rejection of Claims Under 35 U.S.C. §112, Second Paragraph

Claims 13, 16, 19, 23 and 25 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In particular, claims

13, 16 and 19 have been suggested as being confusing for reciting passages drawn to claims of Group IV. The appropriate correction has been made.

The Examiner suggests that claims 23 and 25 are confusing and indefinite in that these claims recite "a means for analyzing a biological sample" for the presence of the RAT gene or RAT mutant gene, wherein the "means" is not identified in the claim. Further, claims 23 and 25 have been deemed indefinite for reciting "the RAT mutant gene" with no antecedent basis for this term earlier in the claim. The specification at page 16, lines 13-16, teaches that a kit of the present invention comprises one or more containers filled with one or more of the ingredients of the agents or pharmaceutical compositions of the invention, wherein an agent is a molecule that interacts with the RAT gene or RAT mutant gene to increase or decrease expression of the RAT gene or RAT mutant gene (see pages 11-12). Accordingly, Applicant has amended claims 23 and 25 to indicate that the respective kits comprise an agent which interacts with a RAT gene of SEQ ID NO:1 or RAT mutant gene of SEQ ID NO:3. In view of these amendments, it is respectfully requested that the rejections of claims 13, 16, 19, 23 and 25 under 35 U.S.C. 112, second paragraph, be withdrawn.

V. Rejection of Claims Under 35 U.S.C. §112, First Paragraph

Claims 13-21 have been rejected under 35 U.S.C. 112, first paragraph, as lacking written description and enablement. The Examiner suggests that the specification does not teach even one agent that inhibits growth or infectivity, or that inhibits expression of the nucleic acid sequence of claim 1. It is

suggested that one of ordinary skill would not know how to make and/or use the invention of the instant claims and furthermore that the artisan would not have at least a reasonable assurance that Applicant had possession of the invention at the time of filing. Applicant respectfully traverses this rejection.

MPEP 2164.01 states the test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. Denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrick GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984). Further MPEP 2164.02 states that *the specification need not contain an example* if the invention is otherwise disclosed in such manner the one skilled in the art will be able to practice it without an undue amount of experimentation *In. re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970).

At the time of filing, library screening was conventional in the art and the instant application provides guidance to the skilled artisan regarding libraries that can be screened (see pages 12-15); the end-point of the screen, *i.e.*, a decrease in the expression of RAT nucleic acid sequences which, based on the activity of RAT, results in the inhibition of growth and increased lysis of bacteria (see paragraph bridging pages 11-12); and types of inhibitory agents which can be identified in the screen (*i.e.*, antisense molecules, ribozymes, means for

introducing mutations, or small organic molecules). As library screening is a mature technology where the level of skill is quite high and advanced, Applicant believes that there is sufficient guidance in the specification to enable one of skill in the art to make and/or use the method of the invention to identify agents which inhibit expression of RAT thereby inhibiting growth and increasing lysis of bacteria. Furthermore, at the time of filing, examples of agents such as antisense molecules directed to specified nucleic acid sequence targets were well-established in the art for use in inhibiting gene expression in bacteria and therefore pathogenesis of bacteria. For example, Ji et al. ((1999) J. Bacteriol. 181(21):6585-90) teach that antisense hla RNA can down-regulate chromosomally-derived hla gene expression *in vitro* and can reduce alpha-toxin expression in two different murine models of *S. aureus* infection thereby eliminating the lethality of the infection. Thus, having the nucleic acid sequence of the RAT gene and the teachings of the instant specification, one of ordinary skill in the art would readily recognize that an antisense molecule to the RAT gene could be screened in accordance with the assay method of the present invention and subsequently used to inhibit expression of the RAT gene thereby inhibiting growth and increasing lysis of bacteria. In an earnest effort to more clearly convey the teachings of the instant specification, Applicant has amended claims 13 and 16 to recite that the agents inhibit growth and increase lysis of bacteria. It is therefore respectfully requested that the rejection of claims 13-21 be withdrawn.

Claims 1-3, 8-10, 13-21, 23 and 25 have been rejected under 35 U.S.C. 112, first paragraph, because it has been suggested

that the specification, while being enabling for SEQ ID NO:1 or SEQ ID NO:3 from *Staphylococcus aureus*, does not reasonably provide enablement for claims of the indicated scope as the specification does not teach any other gene that regulates expression of polypeptides involved in autolytic processes or that any other Rat gene has been isolated from any other source. The Examiner suggests that the specification does not teach one of ordinary skill in the art to obtain nucleic acids of the scope of the instant claims. Applicant respectfully disagrees.

In an earnest effort to facilitate the prosecution of the instant application, Applicant has amended claim 1 to indicate that the isolated nucleic acid encoding a polypeptide which regulates expression of polypeptides involved in autolytic processes in bacteria hybridizes under stringent conditions to a nucleic acid comprising the nucleic acid sequence of SEQ ID NO:1 or SEQ ID NO:3. MPEP 2164 states that the information contained in the disclosure of an application must be sufficient to inform those skilled in the relevant art how to both make and use the claimed invention. Detailed procedures for making and using the invention may not be necessary if the description of the invention itself is sufficient to permit those skilled in the art to make and use the invention. As the level of skill in the art of Southern blot analysis, nucleic acid isolation, and sequence analysis is quite advanced, the teachings of the instant specification would readily enable one of skill in the art to isolate and recognize a RAT gene or RAT gene homolog that hybridizes under stringent conditions (*i.e.*, having at least 60% homology at hybridization conditions of 60°C at 2X SSC buffer; see page 10, lines 22-27) to a nucleic acid comprising the

nucleic acid sequence of SEQ ID NO:1 or SEQ ID NO:3. As disclosed at page 9, lines 3-31, such homologs with significant sequence similarity to the RAT gene were identified in a comparison the RAT gene sequence with the genomes of multiple bacterial genera. Withdrawal of this rejection is therefore respectfully requested.

VI. Rejection of Claims Under 35 U.S.C. §102

Claims 1-3 have been rejected under 35 U.S.C. §102(a or b) as being anticipated by either Brunskill et al. (Reference U); Fujimoto et al. (Reference V), Groicher et al. (Reference W), Brunskill et al. (Reference AA), Fournier et al. (Reference AC), Pinho et al. (Reference AH) and Ramadurai et al. (Reference AI). It is suggested that these references anticipate a nucleic acid from *Staphylococcus aureus* that regulates the expression of polypeptides involved in autolytic processes in bacteria because Brunskill et al. (U) teach a mutant of the *lytS* gene of *S. aureus* that exhibited increased autolysis; Fujimoto et al. teach mutations within the *S. aureus* virulence factor regulatory genes, *agr* and *sar*, affect autolysis; Groicher et al. teach that *S. aureus* LytSR affects murein hydrolase activity and autolysis and that a *lrgAB* mutation enhanced penicillin-induced killing of cells; Brunskill et al. (AA) teach that *S. aureus lrgA* encodes a murein hydrolase supporter, while *lrgB* may encode a protein having murein hydrolase activity; Fournier et al. teach that the *arlS* mutant of *S. aureus* exhibited increased autolysis; Pinho et al. teach that inactivation of *pbpC* from *S. aureus* caused a small but significant decrease in the rates of autolysis; and Ramadurai et al. teach that a gene encoding an autolytic activity was

identified in the autolysis-deficient mutant (Lyt$^-$) of *S. aureus*. Applicant respectfully disagrees.

As indicated *supra*, Applicant has amended claim 1 such that it reads on an isolated nucleic acid encoding a polypeptide which regulates expression of polypeptides involved in autolytic processes in bacteria, wherein the nucleic acid hybridizes under stringent conditions to a nucleic acid comprising the nucleic acid sequence of SEQ ID NO:1 or SEQ ID NO:3. MPEP 2131 indicates that a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Applicant has compared the sequences of the nucleic acids taught in the cited references using BLAST-2 version BLASTN 2.2.10 and finds that these nucleic acid sequences fail to meet the criteria of a nucleic acid sequence that would hybridize under stringent conditions (*i.e.*, having at least 60% homology at hybridization conditions of 60°C at 2X SSC buffer) to a nucleic acid comprising the nucleic acid sequence of SEQ ID NO:1 or SEQ ID NO:3. See Table 1 which shows that the sequences of the cited references share no significant homology with a nucleic acid sequence of SEQ ID NO:1 and, likewise, SEQ ID NO:3 as SEQ ID NO:3 is a truncated version of SEQ ID NO:1.

TABLE 1

Gene Name	Reference Cited	Gene Accession No.	% Homology
LytS	Brunskill et al. (U)	L42945	N.S.
ArgAB	Fujimoto et al. (V)	X52543	N.S.
SarA/R	Fujimoto et al. (V)	U20782/AF207701	N.S./N.S.
LytSR	Groicher et al. (W)	L42945	N.S.

LrgAB	Groicher et al. (W)	U52961	N.S.
LrgAB	Brunskill et al. (AA)	U52961	N.S.
ArlS	Fournier et al. (AC)	AF165314	N.S.
PbpC	Pinho et al. (AH)	AJ243120	N.S.
LytM	Ramadurai et al. (AI)	L77194	N.S.

N.S. - No significant similarity was found.

Accordingly, because the cited references fail to teach each an every element of the claim 1, these references fail to anticipate claim 1 and claims dependent therefrom. It is therefore respectfully requested that this rejection be withdrawn.

VII. Rejection of Claims Under 35 U.S.C. §103

Claims 1-3, 8-10, 13-21 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Brunskill et al. (Reference U); Fujimoto et al. (Reference V), Groicher et al. (Reference W), Brunskill et al. (Reference AA), Fournier et al. (Reference AC), Pinho et al. (Reference AH) and Ramadurai et al. (Reference AI). The Examiner suggests that it would have been obvious to put the gene of the cited references into a transposon, vector, or host cell using known methods and the motivation to do so would be to further study the gene and/or to produce more of the gene or polypeptide encoded thereby. It is suggested that the methods of claim 13-21 would have been obvious in view of the cited references in that they teach genes that are involved in autolysis and therefore the inhibition of infectivity of bacteria by using agents that inhibit the expression of the genes of the cited references would have been obvious. Applicant respectfully traverses this rejection.

As indicated *supra*, the cited references, when alone or combined, fail to teach or suggest a nucleic acid sequence

encoding a polypeptide that would hybridize under stringent conditions (*i.e.*, having at least 60% homology at hybridization conditions of 60°C at 2X SSC buffer) to a nucleic acid comprising the nucleic acid sequence of SEQ ID NO:1 or SEQ ID NO:3. As these reference fail to establish a *prima facie* case of obvious, it is therefore respectfully requested that this rejection be withdrawn.

VIII. Conclusion

The Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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